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PCT Application
PCT/JP2003/007906

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

10/518749

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 03-040-PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP03/07906	International filing date (*day/month/year*) 23 June 2003 (23.06.03)	Priority date (*day/month/year*) 24 June 2002 (24.06.02)
International Patent Classification (IPC) or national classification and IPC C12N 5/06, A61P 25/00, A61K 35/30		
Applicant TANABE SEIYAKU CO., LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23 June 2003 (23.06.03)	31 October 2003 (31.10.2003)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP03/07906

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claim No. 19

because:

☒ the said international application, or the said claim No. 19 relates to the following subject matter which does not require an international preliminary examination *(specify)*:

The invention of claim 19 concerns a method for diagnosing or treating the human body by therapy, which does not require an international preliminary examination by the International Preliminary Examining Authority in accordance with PCT Article 34(4)(a)(i) and Rule 67.1(iv).

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-9	YES
	Claims	10-18	NO
Inventive step (IS)	Claims		YES
	Claims	1-18	NO
Industrial applicability (IA)	Claims	1-18	YES
	Claims		NO

2. Citations and explanations

Document 1
KAWASAKI, H. et al., Generation of dopaminergic neurons and pigmented epithelia from primate ES cells by stromal cell-derived inducing activity.
Proc Natl Acad Sci USA. (January 29, 2002), Vol. 99, No. 3, p. 1580-1585
Document 2
ZHANG, SC. et al., In vitro differentiation of transplantable neural precursors from human embryonic stem cells.
Nat Biotechnol. (2001), Vol. 19, No. 12, p. 1129-1133
Document 3
REUBINOFF, BE. et al., Neural progenitors from human embryonic stem cells.
Nat Biotechnol. (2001), Vol. 19, No. 12, p. 1134-1140
Document 4
KAWASAKI, H. et al., Induction of midbrain dopaminergic neurons from ES cells by stromal cell-derived inducing activity.
Neuron (2000), Vol. 28, No. 1, p. 31-40
Document 5
YOSHIDA, M. et al., Neurotrophic effects of conditioned media of astrocytes isolated from different brain regions on hippocampal and cortical neurons.
Experientia (1995), Vol. 51, No. 2, p 133-136
Document 6
ROUSSELET, A. et al., In vitro regulation of neuronal morphogenesis and polarity by astrocyte-derived factors.
Dev Biol. (1990), Vol. 137, No. 1, p. 33-45
Document 7
PATAKY, DM. et al., Fibroblast growth factor treatment produces differential effects on survival and neurite outgrowth from identified bulbospinal neurons in vitro.
Exp Neurol. (2000), Vol. 163, No. 2, p. 357-372
Document 8
KILPATRICK TJ. et al, The differentiation and survival of murine neurons in vitro is promoted by soluble factors produced by an astrocytic cell line.
J Neurosci Res. (1993), Vol. 35, No. 2, p. 147-161

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V:

Document 9
Neurons and astrocytes influence the development of purified 0-2A progenitor cells.
Glia (1991), Vol. 4, No. 6, p. 559-571

Based on the descriptions in document 1-4 cited in the international search report, the inventions of claims 10-18 lack novelty and an inventive step.

Documents 1-4 describe the derivation of neural stem cells from embryonic stem cells by the SDIA method and the neurosphere method, etc.
They also describe the use of the derived neural stem cells as a medicinal composition.

The inventions of claims 10-18 are also neural stem cells derived from embryonic stem cells, and therefore are indistinguishable from the inventions of documents 1-4.

Based on the descriptions in documents 1-9 cited in the international search report, the inventions of claims 1-9 lack an inventive step.

Documents 5-9 state that astrocyte acclimation medium has the effect on neural stem cells of promoting nerve cell differentiation. Document 7 in particular states that astrocytes produce neural nutritional factors such as FGF-2.

Because it is clear from the descriptions in documents 5-9 that astrocyte acclimation medium contains some factors that promote nerve cell differentiation, persons skilled in the art can easily conceive of using astrocyte acclimation medium in addition to FGF, which is a cytokine used in the SDIA and neurosphere methods, in the SDIA neurosphere methods described in documents 1-4.